
The Role of the Pharmacist in the Anticoagulant Clinic

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Approximately 50,000 patients in Britain receive oral anticoagulant treatment every day and over two million tests of anticoagulant control are performed in a year [1, 2]. Close supervision of the patients is necessary because dose requirements are variable and there is an ever-present risk of drug interactions and even major bleeding [3].

Good anticoagulant control is also influenced by diet, intercurrent illness and poor compliance, and recent reviews suggest that in the UK the standard of control is often inadequate [4-6]. One factor which may lead to inconsistent management is the delegation of responsibility to junior doctors who do not stay long enough in each training post to learn the patients' idiosyncrasies [4, 5].

With the dual objectives of obtaining a consistent standard of anticoagulation control and of bringing the pharmacist more directly into the arena of patient care, an anticoagulant clinic managed jointly by pharmacists and physicians was started in the North Staffordshire Hospital Centre in September 1979. This article describes the management and organisation of such a clinic (the 'combined clinic') and retrospectively compares the results achieved with those obtained by other physicians who retained the supervision of anticoagulant therapy entirely in the hands of medical staff (the 'standard clinics').

Methods

The combined clinic supervises the patients of four consultant physicians and is held twice weekly to run concurrently with the medical clinic of a consultant physician (R.B.C.). The pharmacist has access to the patient's medical file in which anticoagulant control is recorded on a special chart. He counsels the patient, adjusts dosage as necessary, decides when the patient should next attend and dispenses a supply of tablets. To ensure a consistent standard of practice, guidelines (see

Appendix) were prepared for the management of the anticoagulant clinic by pharmacists, based on those used in the Division of Clinical Pharmacy at the University of California, San Francisco (Dr Steven Kayser, personal communication). The pharmacist's decisions are checked and initialled by a doctor at the medical clinic to whom patients may be referred if problems arise. Medical review is otherwise limited to one consultation at three months in the case of patients receiving a short course of anticoagulant therapy, or twice yearly consultations for those on long-term treatment.

The standard clinics are managed as an integral part of the normal medical out-patient clinics. The patients' anticoagulant control is supervised either by the consultant physician or the junior medical staff. The patients are frequently seen by different doctors at successive appointments.

The names of 116 unselected patients who had received anticoagulant therapy during the calendar year 1980 were taken from the laboratory records. Sixty-two patients had attended the combined clinic and 54 had been supervised at standard clinics. The following information was obtained from the patients' medical records: sex, age, weight, smoking history, alcohol consumption, the indication for anticoagulant treatment, biochemical indices of liver and kidney function, dose and duration of heparin therapy, loading dose of warfarin, length of in-patient stay after commencement of warfarin, and duration of anticoagulant therapy. Treatment with drugs known to interact with warfarin during in-patient and out-patient management, evidence of bleeding or other unwanted effects, and factors which might affect control such as poor compliance and intercurrent illness were also recorded.

In this hospital centre warfarin dosage is adjusted by reference to a prothrombin index (PI) which is the reciprocal of the British Comparative Ratio (BCR), expressed as a percentage. The desired therapeutic range was defined as a PI of between 50-30 per cent (corre-

sponding to a BCR of 2-3.3) except for one consultant in the standard clinic group whose chosen range was 40-20 per cent (corresponding to a BCR of 2.5-5).

Anticoagulant control was assessed by several methods.

1. The average interval between appointments was calculated by dividing the total number of weeks for which a patient received treatment by the number of his attendances.

2. The number of occasions on which the PI was above or below the desired therapeutic range (representing under-anticoagulation and over-anticoagulation respectively) was totalled and expressed as a percentage of the total number of PI readings for each group.

3. The degree of fluctuation in PI was determined by averaging the PI changes between one attendance and the next throughout each patient's course of treatment.

The number of patients experiencing unwanted effects from anticoagulation was obtained from reports of these events in the patients' medical records. Unwanted effects sought included bruising, epistaxis, microscopic haematuria, haematemesis, melaena, frank haematuria and further episodes of thrombosis or embolisation. The duration of treatment of single episodes of deep vein thrombosis (DVT) or pulmonary embolism (PE) was compared by calculating the mean duration of therapy for these indications in each group. The comparison was carried out retrospectively, since a prospective study would have influenced the management of the patients so as to invalidate the comparison.

Results

The characteristics of the patients attending the two types of clinic are shown in Table 1. There was no significant

Table 1. Patients studied.

	Cases	
	Combined Clinic	Routine Clinics
Male	24	32
Female	38	22
Age in years (mean and range)	57 (25-77)	52 (23-79)
Weight in kg (mean and range)	72 (46-96)	73 (46-101)
Renal Function*		
Normal	44	32
Abnormal	10	11
Unknown	8	11
Liver Function**		
Normal	43	32
Abnormal	9	14
Unknown	10	8

*Renal function was recorded as abnormal if serum creatinine was outside the normal range.
 **Liver function was recorded as abnormal if two or more liver function tests (plasma bilirubin, aspartate transaminase, lactate dehydrogenase, alkaline phosphatase) were outside the normal range.

difference between the groups in age, weight, or renal and hepatic function. Similarly, Table 2 shows that the two clinics were comparable with regard to the reasons for which anticoagulant therapy was given.

Table 2. Indications for warfarin therapy. DVT—deep vein thrombosis. PE—pulmonary embolism.

Indications	Cases	
	Combined Clinic	Routine Clinics
DVT single	11	13
DVT recurrent	8	6
PE single	25	25
PE recurrent	13	8
Mitral valve disease	3	0
Atrial fibrillation alone	0	1
Heart valve prosthesis	2	1

The average actual duration of anticoagulant treatment for single episodes of DVT and PE and the intended duration of treatment as previously declared by the physicians are shown in Table 3. In all cases the actual

Table 3. Duration (and range) of warfarin therapy. DVT—deep vein thrombosis. PE—pulmonary embolism.

		Weeks of Treatment	
		Combined Clinic	Routine Clinics
DVT (single)	Intended	12	6
	Actual	13.6 (8-26)	8.2 (3-16)
PE (single)	Intended	12	12
	Actual	14.2 (9-29)	12.4 (4-20)

duration was comparable to the intended duration, but it is also apparent from this table that the clinicians of the combined clinic normally maintained anticoagulation for 12 weeks after a single episode of DVT, while those of the routine clinics did so for only six weeks. Table 4 illustrates

Table 4. Control of anticoagulation. PI—prothrombin index.

	Combined Clinic	Routine Clinics
Interval between appointments (weeks)*	1.82 (0.3-4.0)	1.81 (0.3-13.0)
Percentage of PI readings above desired range (under-anticoagulation)	19%	26%
Percentage of PI readings below desired range (over-anticoagulation)	11%	7%
Difference in PI (%) between attendances*	9.93 (0-58)	9.88 (0-59)

*Mean and range

our assessment of the management of therapy by the two types of clinic, both of which achieved a similar average standard of anticoagulant control among their patients with a similar range of variation in frequency of attendance and PI fluctuation. The number of patients experiencing unwanted effects during anticoagulation is

Table 5. Unwanted effects. PE—pulmonary embolism.

Effect	Number of Patients	
	Combined Clinic	Routine Clinics
Bruising	2	0
Epistaxis	1	1
Microscopic haematuria*	17	10
Frank haematuria	1	0
Haematemesis/melaena	1	0
Further PE	0	1
No unwanted effects	40	42
Total	62	54

*Detected by reagent strip urinalysis.

illustrated in Table 5 which indicates no major differences between the two types of clinic. The most common unwanted effect was microscopic haematuria detected by reagent strip urinalysis. One patient in the combined clinic group had frank haematuria while the PI was within the therapeutic range, and one patient with chronic liver disease had melaena while under-anticoagulated (PI 52 per cent), which was subsequently found to be due to gastritis.

Discussion

Oral anticoagulant therapy is sufficiently hazardous to warrant special measures to ensure safe and effective treatment, and continuity of surveillance is an important factor in avoiding mistakes. Our increasing awareness of the problems coincided with the pharmacists' aspiration to become more directly involved in patient care, and the idea of a joint pharmacist/physician anticoagulant clinic was conceived to satisfy these views. The concept of pharmacist responsibility for dosage adjustment of anticoagulants has been tried out in the USA[7-9], and shared responsibility between a physician and a pharmacist working together has been described both in the USA[10] and in Britain[11], but in general such treatment is traditionally managed by doctors. The task of supervising treatment and making dosage adjustments is regarded as fairly simple and commonly falls to junior doctors, who periodically move from one post to the next in order to satisfy training requirements. We believe that continuity of care can more easily be maintained by a pharmacist who is interested in applying his knowledge of pharmacology to the practical treatment of patients.

Before embarking upon so radical a change in established practice it was important to ensure that junior doctors should not lose the opportunity of gaining experience in monitoring oral anticoagulation; and that the statutory requirements for the issue of prescribed drugs by qualified medical practitioners should be met. We considered that the training needs of junior hospital doctors were adequately provided for by the experience they gained in initiating warfarin therapy while the patient was still in hospital; and the statutory need for the prescription of warfarin by a doctor would be satisfied by the shared responsibility of the combined pharmacist/physician anticoagulant clinic, where there would always

be a medical presence and where all warfarin prescriptions advised by the pharmacist would be checked and initialled by a doctor.

Once the new system had been put into practice it became necessary to compare it objectively with the established practice of medically supervised anticoagulant therapy running concurrently. The results of this comparison between similar groups of patients receiving warfarin therapy for similar indications show that in both sorts of clinic there was considerable variation in the duration of therapy, which was sometimes as much as two months shorter or three months longer than the intended duration. The more extreme variations were due to compliance failure (2 cases), to an alteration in the diagnosis (2 cases), to persistence of the underlying condition which had led to thromboembolic disease such as prolonged immobilisation (2 cases), or to unexplained decisions on the part of the supervising doctors to prolong or cut short treatment (5 cases). These variations were seen equally in the combined and standard clinics, and it was clear that the duration of anticoagulant treatment for a single episode of DVT or pulmonary embolism varied considerably from one physician to the next, lying between six weeks and six months. In the combined clinic we now ask clinicians to state the intended duration of treatment at the outset and the pharmacist draws it to the clinician's attention if treatment appears to be running on too long, but the decision to stop treatment rests always with the clinician and would be taken at a medical follow-up attendance, depending on the medical assessment of that patient's need. The routine three-month medical appointment is intended to prevent inadvertent prolongation of treatment, but a clinician could always decide whether it should be cut short or prolonged according to the clinical situation. The general standard of anticoagulant control and the degree of fluctuation in prothrombin index were the same in both combined and standard clinics, and the low incidence of unwanted effects was common to both groups of patients. It should be borne in mind that the comparison was made retrospectively, so that the usual practice of the participating doctors and pharmacists was not modified by a feeling of being overlooked.

Our experience in the combined clinic showed that the pharmacist never had any hesitation in consulting his medical colleagues, and would do so, on average, once in 25 patient attendances. Since the doctor and the pharmacist worked in adjoining rooms access between them was easy, and if the patient complained of any symptoms unrelated to the anticoagulant treatment the pharmacist automatically sought medical advice without further ado.

On the strength of these observations it cannot be said that the results obtained by the pharmacist and physician working together were better or worse than the standard clinics managed by clinicians alone, and no significant cost benefit is obtained by substituting a pharmacist to do this work in place of a junior doctor. Critics have argued that the additional cost of assigning a staff pharmacist for 4 hours per week to this role is not justified in the absence of objective evidence of an improvement in the service provided, but this criticism overlooks the subjective bene-

fits of the combined pharmacist/clinician clinic which we observed, namely:

1. Dual participation reduces the risk of mistakes.
2. Medical confidence is increased by a system in which the supervision is carried out by a pharmacist with continuing responsibility.
3. The pharmacist's professional role is enhanced.

We believe that these are significant benefits, and efforts are being made to expand the clinic to cope with requests for access from other groups of clinicians. The service is limited at present to those physicians whose clinics happen to coincide with the pharmacist's availability, because the essential principle of this concept is that the pharmacist who runs the clinic should always have at hand a clinician who is responsible for the patients' care.

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APPENDIX: MANAGEMENT OF THE ANTICOAGULANT CLINIC BY PHARMACISTS

Objectives

The objective for pharmacists who are responsible for warfarin anticoagulation therapy is to achieve consistent management and surveillance of therapy in order to promote maximum effectiveness of the drug and minimal risk from adverse effects and over-dosage.

Rationale

Close supervision of warfarin therapy is considered necessary for the following reasons:

1. Warfarin exhibits pronounced inter-individual elimination kinetics. This variation is primarily ascribed to differences in the amount of free fraction of the drug in the serum.
2. There are many drugs, both prescription and over-the-counter preparations, which can produce clinically important interactions with warfarin.
3. There are many diseases which can alter the pharmacological response to warfarin.
4. The major unwanted effect of warfarin — bleeding — is a highly dangerous one.
5. Elderly patients are particularly at risk from problems associated with warfarin therapy because they commonly suffer from more than one disorder and are receiving several drugs.

Methods

Organisation of the Clinic

- (a) On the appointment date the patient will first report to the Haematology Department for a prothrombin test.

The result of the test will be entered in the patient's copy of the DHSS Anticoagulant Treatment Booklet by the haematologist. The patient will then report to the Anticoagulant Clinic and the result of the prothrombin test will be transferred by the pharmacist to the Anticoagulant Treatment Chart (Fig. 1). The Anticoagulant Treatment Chart will remain permanently in the patient's notes.

- (b) The patient's warfarin dosage will be determined by the pharmacist and will be entered on the Anticoagulant Treatment Chart and also in the patient's Treatment Booklet. The entry in the Treatment Chart will be regarded as a prescription and a physician's signature will be obtained before a supply of warfarin is dispensed.

- (c) The dispensing of the patient's supply of warfarin will take place at the clinic. The completed prescription will be checked by the pharmacist and the Treatment Booklet will be returned to the patient.

- (d) All supplies of containers, labels and warfarin tablets will be obtained from the central out-patients pharmacy department by the pharmacist before commencement of the clinic. These supplies will be returned to the pharmacy department for safe-keeping at the end of each clinic.

General Responsibilities

- (a) The pharmacist shall assist the physician in the management of patients on warfarin.

- (b) The pharmacist will adjust warfarin dose when indicated, maintain a record of this information, and educate the patient concerning the use of warfarin.

- (c) The aim of anticoagulation therapy with warfarin is to maintain a prothrombin index (PI) of between 30 and 50

- (v) Addition or cessation of any concurrent medication (this may be recorded in the 'comments' section of the Anticoagulation Treatment Chart).
- (c) If there has been a significant increase or decrease of the prothrombin time to a value considered out of control, the following questions are asked of the patient in order to determine the cause of the prothrombin time change:
 - (i) Has the patient started or stopped taking any other medication, including proprietary drugs?
 - (ii) Has there been a change in the patient's alcohol consumption?
 - (iii) Have any other illnesses developed such as infection, acute hepatitis, diarrhoea, CCF, etc?
 - (iv) Is the patient taking the warfarin correctly, i.e. correct dose, omission or addition of doses?
 - (v) Has the patient developed fever?
 - (vi) Has the patient altered his diet significantly?
- (d) Based on what has been determined to be the cause of the prothrombin time change, the pharmacist, if neces-

sary in consultation with the physician, will decide on further warfarin therapy. The pharmacist will convey this information to the patient.

(e) In the event of the patient being admitted to hospital, the pharmacist will make at least one check on the patient's anticoagulation therapy. A brief summary of the admission will be indicated in the Anticoagulant Treatment Chart.

(f) Discharge from the Anticoagulant Clinic will occur after adequate duration of therapy, or where the risks of therapy are considered greater than the benefits, or at the request of the patient, on the decision of the physician.

Acknowledgement

This appendix is adapted from a document produced by Dr Steven Kayser, Associate Clinical Professor in the Division of Clinical Pharmacy at the University of California, San Francisco.

A Plagiarist Plagiarised

When the *De Fabrica* was published in 1543, Vesalius had obtained what privileges he could which theoretically prevented anyone from reprinting his book on much of the continent; but he appears to have failed to do the same for England, or else had not thought it necessary. Imagine his dismay, therefore, when two years later there was published in London a work which borrowed not a few, but a majority of the illustrations from the *De Fabrica*, as well as some from the *Epitome—Compendiosa totius anatomiae delineatio, aere exarata: per Thomam Geminum*—a title which refers only to the engravings, the text being added perhaps as an afterthought. This Thomas Geminus, also known as Lambrit, came from Flanders, and besides being an engraver, was an empiric, a printer, and a maker of mathematical instruments. His manual of anatomy contains some of the earliest copper plate engravings to have appeared in England; its publication may have induced Geminus to practise medicine and surgery. In consequence he was prosecuted by the College for practising without a licence, and fined. John Caius, who was President at the time, was asserting the right of the College to extend its authority over the whole coun-

try; to this end he armed its agents with a letter which Geminus had undertaken to print in remission of his fine. This was in 1556.

Three years later (1559) the second edition of an English translation of his manual was published. There are two copies in the College library, one of which belonged to a George Frederick Boyd, whose identity presents something of a puzzle. An apothecary of this name served in the 84th Regiment, and in the American War of Independence, and died at Basingstoke in 1801; a surgeon of the same name also served in the 84th Regiment, but died at Halifax in 1789. The previous owner was John Patch, a surgeon of Exeter. An interesting note in his hand written 20th May 1728 reads: 'The first Edition of this Book (formerly in my Study) was publish'd in Latin by the same Author at London An^o 1545 under the following title *Andreae Vesalii Bruxellensis suorum de Humani Corporis Fabrica Librorum Epitome*: this was about two years after that Vesalius obliged the World with his first and one of the famous Basil Editions of his Anatomy, with wooden Cutts, whereof, I think, these are very good Copyes.' This 'title' is in fact

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